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FDA Decision On Interchangeable Exclusivity Allows Pfizer To Rival Boehringer On Adalimumab

Humira Biosimilar Abrilada Is Now Interchangeable; Pfizer Reveals Launch And Pricing Details

by David Wallace

An FDA decision around the timing of first interchangeable biosimilar exclusivity has brought to an end Boehringer Ingelheim's time on the market with a unique interchangeable Humira rival, with the agency also granting interchangeability for Pfizer's Abrilada version of adalimumab.

A US Food and Drug Administration decision around the timing of exclusivity for first interchangeable biosimilars has resulted in Pfizer being awarded an interchangeability designation for its Humira (adalimumab) rival, barely three months after the first interchangeable biosimilar from Boehringer Ingelheim hit the market.

Biosimilars designated as interchangeable in the US – meaning they can benefit from pharmacy-level substitution, subject to state law – can expect to enjoy a year of exclusivity for their interchangeability designation if they are the first biosimilar of a given product to be deemed interchangeable by the FDA.

However, Pfizer's Abrilada (adalimumab-afzb) has now been approved as a second interchangeable biosimilar to Humira, after Boehringer Ingelheim's Cyltezo (adalimumab-adbm) – which was approved as interchangeable in late 2021 but was only recently launched as part of

Key Takeaways:

- The US FDA has approved Pfizer's

a second wave of Humira competition in July. (Also see "*First Interchangeable Humira Biosimilar Approved In US*" - Generics Bulletin, 18 Oct, 2021.) (Also see "*Fresh Wave Of Adalimumab Biosimilars Hits US*" - Generics Bulletin, 3 Jul, 2023.)

Pfizer – which did not launch its approved Abrilada adalimumab biosimilar along with the large group of rivals that hit the market in July following Amgen's debut of biosimilar competition in January – is now expecting to introduce its interchangeable version this month, with the company by the end of the year planning to adopt a dual pricing strategy in common with several other adalimumab biosimilars.

Abrilada (adalimumab-afzb) as an interchangeable biosimilar to Humira. Launch is expected this month.

- This marks the second Humira biosimilar to be approved as interchangeable, after Boehringer Ingelheim's Cyltezo (adalimumab-adbm).
- First interchangeable biosimilars are meant to benefit from a year of interchangeable exclusivity – but Cyltezo has only been on the market since July.
- The news comes shortly after Boehringer Ingelheim confirmed launch of an unbranded version of Cyltezo at a much lower price point.

"Abrilada will be available later this year at two price points, with the goal of achieving the broadest possible access for patients," Pfizer stated. "Starting in late October 2023, Abrilada will be available at a list price (wholesale acquisition cost) 5% below the Humira list price. Later in 2023, Abrilada will be available at a second list price 60% below the Humira list price."

Abrilada's interchangeable designation applies to all approved indications of the biosimilar, including rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa and uveitis.

The designation was supported by data from Pfizer's Phase III REFLECTIONS B538-12 study, which demonstrated similar outcomes in terms of pharmacokinetics, safety and immunogenicity in patients with moderately to severely active RA who switched multiple times between treatment with the 40mg/0.8ml concentration of Abrilada and the 40mg/0.4ml concentration of Humira, compared to patients who received continuous Humira, each taken in combination with methotrexate. (Also see "*FDA To Review Pfizer's Abrilada For Humira Interchangeability*" - Generics Bulletin, 3 Mar, 2022.)

Other than Abrilada and Cyltezo, no further adalimumab biosimilars have yet been approved as interchangeable by the FDA.

Pfizer had already previously told *Generics Bulletin* in early 2023 that the FDA had "completed their review and provisionally [Pfizer's emphasis] determined that Abrilada meets the standards as an interchangeable biosimilar to Humira," suggesting that Cyltezo's exclusivity was the only barrier to an interchangeability designation. (Also see "*Provisionally Interchangeable? FDA Weighs 'Requirements' For Pfizer's Adalimumab*" - Generics Bulletin, 27 Feb, 2023.)

And now asked whether the launch timing related to the interchangeability approval, a Pfizer spokesperson told *Generics Bulletin* that "this launch timing is not related to interchangeability."

Commenting as Pfizer announced the latest developments, Angela Hwang – chief commercial officer and president of Pfizer's global biopharmaceuticals business – said "Abrilada was developed with patients in mind, and having an interchangeable designation is a key step toward potentially increasing their access to this important treatment option."

"With 15 years of global in-market experience in biosimilars and an industry-leading seven marketed biosimilar products in the US," Hwang added, "Pfizer continues to expand options for patient care by introducing Abrilada."

Pfizer has previously indicated that it expects to gain a "fair" share of the adalimumab market with Abrilada. "We are optimistic about the uptake of biosimilars," Hwang said in 2022, suggesting based on Pfizer's experience with Inflectra (infliximab-dyyb) and its oncology biosimilars that "physicians and institutions have become extremely comfortable with the use of biosimilars."

"I think we're very far from where we were when we first launched our first biosimilar here in the US," she highlighted. "That, coupled with the interchangeability data, should mean that we would be able to gain a fair market share." (Also see "*Pfizer Anticipates 'Fair' Share Of Adalimumab Market In US*" - Generics Bulletin, 5 May, 2022.)

FDA Rules On First Interchangeable Biosimilar Exclusivity Unclear

The approval of a second interchangeable Humira rival, just a few months after the launch of the first approved interchangeable adalimumab biosimilar, highlights the lack of clarity around how the first interchangeable exclusivity incentive is expected to function – especially in the continuing absence of long-awaited dedicated FDA guidance on the subject. (Also see "*Biosimilars: US FDA Developing Guidance For First Interchangeable Exclusivity*" - Generics Bulletin, 20 Nov, 2020.)

The agency's Purple Book database of biologics states only that a "first interchangeable exclusivity date" indicates the date that a first interchangeable product's period of exclusivity ends, "which is the date that FDA may make a determination that a second or subsequent biological product is interchangeable with the reference product against which the first

interchangeable biological product was evaluated for any condition of use."

It also notes that "the presence of 'Date TBD' in the Purple Book indicates that FDA has determined that the listed biological product is eligible for first interchangeable exclusivity, but FDA has not yet determined the applicable period of exclusivity."

As recently as September, Cyltezo's first interchangeable exclusivity date in the Purple Book was still listed as "Date TBD".

Speaking to *Generics Bulletin* after the Pfizer approval was made public, Stephen Pagnotta – executive director and biosimilar commercial lead at Boehringer Ingelheim – confirmed that "yes, the FDA has determined the interchangeability exclusivity period for Cyltezo has expired."

"It was unclear how the FDA would interpret and implement first interchangeability exclusivity; including when the period of first interchangeability exclusivity commences," Pagnotta indicated.

"But we have always known that other Humira biosimilars could eventually be granted this designation. We are supportive of a competitive market for biosimilars, where patients have options and more access to biologic medicines."

Earlier this year, Pagnotta had pointed to Boehringer's unique position in the US market thanks to its interchangeability designation (*see sidebar*).

Boehringer Ingelheim's Pagnotta Talks Adalimumab And Interchangeability

By David Wallace

04 Jul 2023

As Boehringer Ingelheim launches the first – and so far, only – interchangeable US adalimumab biosimilar, the firm's biosimilar commercial brand lead Stephen Pagnotta talks to *Generics Bulletin* about how the interchangeability designation puts the firm in a unique position when it comes to competing with Humira.

Read the full article here

Cyltezo was initially launched at just a 5% discount to Humira, compared to deep discounts offered by many other Humira biosimilars. However, within the last week – just ahead of Pfizer publicly announcing Abrilada's interchangeability designation – Boehringer revealed that it was bringing forward the launch of an unbranded version of Cyltezo at a much steeper 81% discount. (Also see "*Boehringer Accelerates Adalimumab Dual Pricing Strategy With 81% Discount*" - Generics Bulletin, 5 Oct, 2023.)

It remains to be seen what further light will be shed on the timing of first interchangeable biosimilar exclusivity by the FDA.

Emphasizing the potential complications for sponsors in an interview with *Generics Bulletin* last year, Samsung Bioepis' Gillian Woollett noted that "in theory, the incentive was to encourage people to seek the designation. But it doesn't block another biosimilar being approved, it only blocks another interchangeable being approved during that window of the exclusivity. So, what becomes key is when does that window start?"

"There seem to be various interpretations," she indicated, "because back during the negotiations – and I was there at many of them – there was no awareness of delays post-approval before launch. So that becomes fundamental to whether the incentive even exists if the exclusivity has been burned through before anybody launches." (Also see "*Cutting Through The Confusion On US Biosimilar Interchangeability*" - Generics Bulletin, 5 Aug, 2022.)